WHAT ARE THE EFFECTS FROM CONTROLLED EXPOSURE TO SPECIFIC SOURCES?

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research and development

Science Question

It is unclear which types of PM sources, as well as components, contribute to the induction of various cardiopulmonary health effects. One approach to examining this issue is to determine whether controlled exposures of appropriate biological systems to source specific PM can induce health effects or responses related to health effects.

Systems utilized for research include:
- cell culture (pulmonary, vascular, and cardiac)
- animal models representing sensitive subpopulations
- human volunteers.

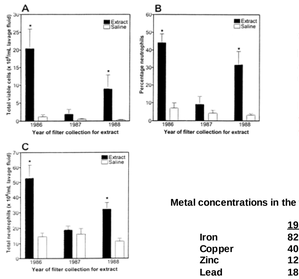
Exposures have ranged from generation of fresh total exhaust, such as diesel exhaust, to surrogates of point source PM such as ROFA. Additionally, the influence of gaseous co-pollutants on the responses observed with PM alone can be determined.

Research Goals

- Identify health effects associated with specific PM sources.
- Identify subpopulations that are susceptible to specific sources.
- Compare relative potencies and efficacies of different PM sources.
- Begin to examine effects associated with combinations of sources.

Steel Plant Emissions

Human Instillation Studies



Volunteers instilled with filter extracts (500 µg) from Provo, and lavaged 20 hr later. Panel A: steel plant operational; Panel B: plant closed; Panel C: plant operational.

Lung inflammation associated with the years that the plant was operating (1986 & 1988) and transition metal content.

Metal concentrations in the three PM extracts from Utah Valley (ng metal/mg extract)

	1986	1987	1988
Iron	82.2	14.8	257.5
Copper	402.8	29.1	471.8
Zinc	1276.5	20.2	690.2
Lead	186.6	5.7	286.7
Nickel	17.6	3.8	11.0
Vanadium	6.0	7.4	37.7

SOURCES EXAMINED

Diesel Exhaust PM

Human Exposure Studies

Human Susceptibility: DEP exposure sensitizes nasal responses to ragweed allergen; -GSTM1 individuals have greater responses

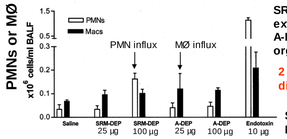
Response as DEP+allergen/allergen

	-GSTM1	+GSTM1
IgE	15.4	5.6
histamine	5.8	3.5

Allergen + DEPM nasally instilled; nose lavaged 24 hr later

Rodent Exposure Studies

DEP Bioactive Components



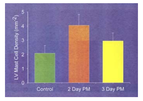
SRM 2975-DEP 5% extractable organics
A-DEP 50% extractable organics

2 DEPM types induce different responses

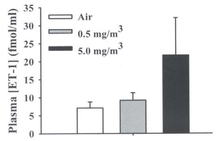
SRM=Std Ref. Material NIST

On road study with freshly generated diesel truck exhaust

Cardiovascular changes noted (see poster presented by Oberdorster)



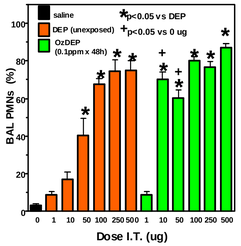
DEP inhalation increases rat cardiac Mast Cells
NIST SRM 2975 (4.5 mg) nebulized 30 min/day
Mast cells may be involved in cardiac toxicity with DEP



DEP inhalation increases rat vasoconstriction via an increase in Endothelin-1 (ET-1)

DEP can induce vascular, cardiac toxicity

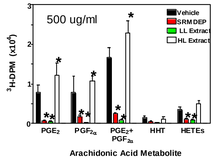
Gaseous co-pollutant can affect the potency of DEP



Rats instilled with DEP, or DEP exposed to 0.1 ppm ozone, and lavaged 24 hr later. [Doses 1-500 µg i.t.]

Diesel exhaust collected in cooled PBS in impingers from high (~75%) and low (~0%) loads. Extracts were normalized for mass, and epithelial cells incubated for 24 hr. Tritiated PGs, derived from cells prelabelled with 3H-AA were measured by HPLC. [SRM DEP was 2975.]

In Vitro Exposure Studies



-Epithelial Inflammation Mediators with DEPs from High vs Low Loads

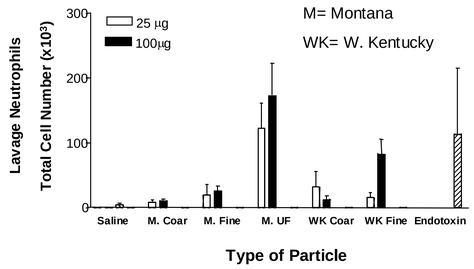
-Viral Infectivity of Epithelial Cells

-Genomics (MØ, endothelial cells)

Diesel extract collected at high load induced more prostaglandins than extract from a low load.

Coal Oil Fly Ash

Mice underwent reflex aspiration of PM; lavaged 18 hr later



Smaller PM have more potency; potency associated with S and trace elements

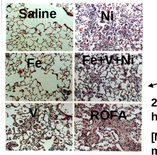
Conclusions/Future Directions

- Biological effects were in a variety of assay systems have been demonstrated with PM derived from several different sources.
- Different sources elicited different responses.
- However, other specific ambient PM sources (e.g., natural gas, gasoline) remain to be studied.
- Studies in which humans are exposed to diesel exhaust are currently in progress. These studies should provide better characterization of health effects and susceptible populations.
- Studies are also in progress using exposure to source pollutants with recently validated appropriate animal models (e.g., ApoE-/- and Brown Norway rats) which may better predict PM-induced cardiovascular and allergic responses.
- Similarly-designed studies will be used to determine effects from other PM sources, such as gasoline and woodsmoke.
- Similar study approaches can be utilized to examine effects of exposure to PM sources that are subject to changing technology, e.g., new compression and spark ignition engines.

Impact and Outcomes

- These findings will provide important information about the health effects associated with exposure to specific sources.
- This "bottom up" approach is complementary to the "top down" approach in which statistical approaches are used to link health effects associated with exposure to ambient PM with specific components and sources present in the PM (see poster presente by Godleski).
- A combination of both approaches should provide the OAR with important information it needs to determine if regulations should be targeted to specific sources of PM.

Residual Oil Fly Ash



ROFA induces Lung & Cardiac Toxicity

2.5 mg ROFA i.t. /300 g rat 96 hr post i.t.

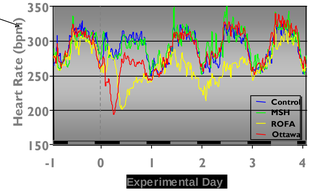
[Metals @ concentration in 2.5 mg ROFA]

Whole ROFA more potent than the major transition metals;

In Vitro Exposure Studies:
Cardiac Myocytes: Inflammation, Ca+2 fluxes
Lung epithelial cells: Inflammation
Lung MØ: Immume suppression

ROFA more potent than an urban PM

Rats i.t. instilled with PM; HR monitored 0-96 hr



MSH= Mt St Helens' PM=2.5 mg i.t. ROFA=0.5 mg i.t.
Ottawa= ambient PM=2.5 mg i.t.

Source to Health Outcome